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10/008,571	12/03/2001	Ian Tomlinson	8039/1125	6655

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EXAMINER
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STEELE, AMBER D

ART UNIT	PAPER NUMBER
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1639

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05/03/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/008,571

Applicant(s)

TOMLINSON ET AL.

Examiner

Amber D. Steele

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 February 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 11, 17 and 54-64 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11, 17 and 54-64 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☒ Certified copies of the priority documents have been received in Application No. 09/888,313.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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### **DETAILED ACTION**

1. The examiner of record for the present application has changed. However, the Technology Center (TC1600) and Art Unit (AU1639) remain the same. The present Office action is non-final.

#### ***Status of the Claims***

2. The amendment to the claims received on July 10, 2006 canceled claims 1-10, 12-16, and 18-53 and amended claims 11 and 17.

The amendment to the claims received on February 2, 2007 added new claims 54-64.

Claims 11, 17, and 54-64 are currently pending and under consideration.

#### ***Priority***

3. The present application claims status as a CIP of U.S. application 09/888,313 filed June 22, 2001 and benefit of U.S. provisional application 60/246,851 filed November 8, 2000. The present application also claims foreign priority to UK 0015443.5 filed June 23, 2000 and UK 0026099.2 filed October 25, 2000.

#### ***Specification***

4. The disclosure is objected to because of the following informalities: the citation for the de Wildt reference on page 55 contains a typographical error. The citation should be de Wildt et al. Nature Biotechnology 18(9): 989-994, 2000 (please note the correct volume number).

Appropriate correction is required.

#### ***Invention as Claimed***

5. The presently claimed invention is drawn to a method for creating two- or three-chain polypeptides comprising providing an array/solid surface that includes a first repertoire of single-

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chain polypeptides in a first series of continuous lines that do not intersect and a second repertoire of single-chain polypeptides in a second series of continuous lines that do not intersect wherein each line of the first series of lines intersects each line of the second series of lines such that members are juxtaposed thereby generating a two-chain polypeptide and a third repertoire of single-chain polypeptides on the array in a third series of continuous lines that do not intersect each other wherein each line of the third series of lines intersects with the first and second series of lines thereby generating a three-chain polypeptide and variations thereof.

#### **Withdrawn Rejections**

6. The rejection of claim 11 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicants arguments.

7. The rejection of claim 17 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicants arguments.

#### ***Claim Rejections - 35 USC § 112***

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 11, 17, and 54-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "continuous lines" in claims 11 and 17 is a relative term which renders the claim indefinite. The term "continuous line" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art

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would not be reasonably apprised of the scope of the invention. The present specification defines a line as preferably "XX long and YY wide" which can be straight, curved, circles, polygons, radial lines, stream, channel, flow, tubes, tubing, droplets which coalesce, spray, tube with a lumen (please refer to page 4, last paragraph; page 5, page 26, first paragraph). The dimension of "XX" and "YY" would not be readily ascertained by one of skill in the art. For example, a "line" "XX long and YY wide" made of "a series of droplets" that "coalesce" into a "circle" could be a spot; a line could be a centrifuge "tube" with a "lumen into which a member of a repertoire useful in the inventions is placed"; a line could be a streak on a plate, a line could be a lane in a gel, etc.

In addition, the term "juxtaposed" in claims 11 and 17 is a relative term which renders the claim indefinite. The term "juxtaposed" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The present specification defines juxtaposition as including "but not limited to physical contact"; separated by no more than 20  $\mu\text{m}$ , 10  $\mu\text{m}$ , or 5  $\mu\text{m}$ ; or intersection of lines wherein the lines intersect at between  $1^\circ$  and  $179^\circ$  angle,  $45^\circ$  and  $135^\circ$  angle,  $90^\circ$  angle. For example, a line (e.g. spot) dropped on top of another spot is "juxtaposed" at an angle; a microcentrifuge tube placed within 20  $\mu\text{m}$  of another tube is "juxtaposed", a streaked plate with colonies along the streak are juxtaposed, a lane in a gel within 20  $\mu\text{m}$  of another lane could be juxtaposed, etc.

#### ***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 11, 17, and 64 are rejected under 35 U.S.C. 102(b) as being anticipated by Bussow et al. Nucleic Acids Research 26(21): 5007-5008, 1998.

For present claims 11, 17, and 64, Bussow et al. teach a picking/gridding robot that gridded onto filter membranes cells expressing proteins (e.g. first, second, and/or third repertoire of single-chain polypeptides, lines on grid from left to right and/or second repertoire of single-chain polypeptides, lines on grid from top to bottom; juxtaposed; antigen) and adding a “stream” (e.g. line; first, second, and/or third repertoire of single-chain/two-chain polypeptides) of monoclonal antibody thus creating two- or three-chain polypeptides (please refer to entire disclosure particularly page 5007, third and fourth paragraphs; page 5008, third full paragraph).

Therefore, the presently claimed invention is anticipated by the teachings of Bussow et al.

12. Claims 11, 17, 54-56, 59-61, and 64 are rejected under 35 U.S.C. 102(b) as being anticipated by Rowe et al. Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS).

For present claims 11, 17, 54-56, 59-61, and 64, Rowe et al. teach methods of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor wherein vertical channels comprise antibodies and adding samples flowed through horizontal channels (e.g. single-chain polypeptides; first repertoire and/or second repertoire; continuous lines that may be at 179° angles if two single-chain polypeptides per channel to make VH-VL for

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example) wherein the vertical and horizontal channels are at 90° angles (please refer to entire reference particularly Figure 1; experimental section).

Therefore, the presently claimed invention is anticipated by the teachings of Rowe et al.

***Claim Rejections - 35 USC § 103***

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. Claims 11, 17, and 54-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rowe et al. Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS) and Stevens et al. U.S. Patent 6,485,943 filed March 22, 1999.

For present claims 11, 17, 54-56, 59-61, and 64, Rowe et al. teach methods of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor wherein vertical channels comprise antibodies and adding samples flowed through horizontal channels (e.g. single-chain polypeptides; first repertoire and/or second repertoire; continuous lines that may be at 179° angles if two single-chain polypeptides per channel to make VH-VL for example) wherein the vertical and horizontal channels are at 90° angles (please refer to entire reference particularly Figure 1; experimental section).

However, Rowe et al. does not specifically teach making VH-VH or VL-VL two-chain polypeptides or the VH-VH or VL-VL two-chain polypeptides bound to antigen to make three-chain polypeptides.

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For present claims 57-58 and 62-63, Stevens et al. teach methods of making recombinant antibody subunit dimers including VH-VH and VL-VL and screening against antigen comprising providing VH and/or VL and interacting the VH and/or VL (please refer to entire specification particularly abstract; column 4, lines 44-67; column 5, lines 1-9; column 6, lines 20-41; column 7, lines 23-36; columns 9-10).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor taught by Rowe et al. with the VH-VH or VL-VL taught by Stevens et al.

One having ordinary skill in the art would have been motivated to do this because Rowe et al. teach that immunosensors are easy to use, provide rapid assay times, have sensitivity comparable to ELISA, and can be utilized to study multianalyte binding (please refer to introduction and conclusion sections). In addition, Stevens et al. teach homologous dimerization of antibody subunits and altering amino acid sequences in the interfacial segments to improve yields of Fab and Fv products and studying the interactions via dimerization assays/screens (please refer to columns 4-5).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the method of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor taught by Rowe et al. with the VH-VH or VL-VL taught by Stevens et al. because Rowe et al. teach utilizing immunosensors to study multianalyte interactions (e.g. VH, VL, antigen, dimmers, trimers; please refer to conclusion).



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Therefore, the modification of the method of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor taught by Rowe et al. with the VH-VH or VL-VL taught by Stevens et al. render the instant claims *prima facie* obvious.

### ***Double Patenting***

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 11, 17, and 54-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of copending Application No. 10/161,145. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the present invention and the invention of U.S. application 10/161,145 are drawn to methods comprising arraying a plurality of polypeptides on a support which can be single-chain or two-chain, arraying a second plurality of polypeptides/targets on a support which can be single-chain, and juxtaposing the supports so that either two-chain or three-chain polypeptides are produced (please note: three-chain polypeptides

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read on antibodies bound to antigens as defined in the present specification; two-chain polypeptides read on scFv bound to antigen).

For present claims 11, 17, and 54-64, U.S. application 10/161,145 claim immobilizing target molecules on a first support wherein the target molecules can be protein, polypeptide, amino acid, whole cell or cell extract (e.g. antigen, single-chain polypeptide, VH, VL), arraying a plurality of polypeptides on a second support wherein the polypeptides can be antibodies (e.g. VH, VL, VH-VL, VH-VH, VL-VL), juxtaposing the first and second supports wherein binding can occur (e.g. making a two-chain or three-chain polypeptide library; please refer to claims 1-18).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Claims 11, 17, and 54-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 11-14, and 42 of copending Application No. 10/161,144. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed invention and the invention as claimed in U.S. application 10/161,144 are drawn to methods comprising arraying immunoglobulin superfamily repertoires on a solid support (e.g. single-chain or two-chain polypeptides and contacting the arrayed repertoire with a target ligand (e.g. juxtaposed, single-chain polypeptides, producing either two-chain or three-chain polypeptides; please note: three-chain polypeptides read on antibodies bound to antigens as defined in the present specification; two-chain polypeptides read on scFv bound to antigen).

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For present claims 11, 17, and 54-64, U.S. application 10/161,144 claims arraying an immunoglobulin superfamily repertoire on a solid support wherein the immunoglobulin repertoire can be VH, VL (e.g. single-chain polypeptide, two-chain polypeptide, scFV, VH-VL, VL-VL, VH-VH), contacting the arrayed repertoire with target ligand wherein the target ligand can be VL (e.g. antigen, scFV, VH, etc.), and allowing binding to produce two-chain or three-chain polypeptides (please refer to claims 1-8, 11-14, and 42).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. Claims 11, 17, and 54-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 11/413,427. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed invention and the invention as claimed in U.S. application 11/413,427 are drawn to methods comprising arranging a first repertoire in at least one first series of continuous lines, arranging a second repertoire in at least one second series of continuous lines forming an array wherein the first and second lines intersect thereby juxtaposing the first and second repertoires (please note: three-chain polypeptides read on antibodies bound to antigens as defined in the present specification; two-chain polypeptides read on scFv bound to antigen).

For present claims 11, 17, and 54-64, U.S. application 11/413,427 claims a method comprising arranging a first repertoire in at least one first series of continuous lines wherein the first repertoire can be VH or VL, arranging a second repertoire in at least one second series of

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continuous lines wherein the second repertoire can be VH or VL, forming an array wherein the first and second lines intersect thereby juxtaposing the first and second repertoires, optionally contacting the array with target (e.g. antigen), and allowing binding to create two- or three-chain polypeptides (please refer to claims 1-23).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

19. Claims 11, 17, and 54-64 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 56-68 and 78-86 of copending Application No. 09/888,313 (please note: a notice of allowance has been mailed however the Patent has not been issued yet, therefore the rejection is still provisional at this time). Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed invention and the invention as claimed in U.S. application 09/888,313 are drawn to methods comprising arranging a first repertoire in a series of continuous lines, arranging a second repertoire in a series of continuous lines, and forming an array via intersecting the lines and juxtaposing the first and second repertoires (please note: three-chain polypeptides read on antibodies bound to antigens as defined in the present specification; two-chain polypeptides read on scFv bound to antigen).

For present claims 11, 17, and 54-64, U.S. application 09/888,313 claims a method comprising arranging a first repertoire in a series of continuous lines wherein the first repertoire can be VH or VL, arranging a second repertoire in a series of continuous lines wherein the second repertoire can be VH or VL, optionally, forming an array via intersecting the lines and

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juxtaposing the first and second repertoires, and optionally contacting the array with a target epitope (e.g. antigen, forming two- or three-chain polypeptides; please refer to claims 56-68 and 78-86)

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Conclusion***

20. The art made of record and not relied upon is considered pertinent to applicant's disclosure. Antibody arrays for high-throughput screening of antibody-antigen interactions, de Wildt et al. Nature Biotechnology 18: 989-994, 2000.

### ***Future Communications***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ADS

April 27, 2007



MARK L. SHIBUYA  
PRIMARY EXAMINER